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Early management of patients with aneurysmal subarachnoid hemorrhage in a hospital without neurosurgical/ neuroendovascular facilities: a consensus and clinical recommendations of the Italian Society of Anesthesia and Intensive Care (SIAARTI)

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Abstract

Background: The immediate management of subarachnoid hemorrhage (SAH) patients in hospitals without neurosurgical/neurointerventional facilities and their transfer to a specialized center is challenging and not well covered in existing guidelines. To address these issues, we created a consensus of experts endorsed by the Italian Society of Anesthesia and Intensive Care (SIAARTI) to provide clinical guidance.

Methods: A multidisciplinary consensus panel composed by 19 physicians selected for their established clinical and scientific expertise in the acute management of SAH patients with different specializations (anesthesia/intensive care, neurosurgery and interventional neuroradiology) was created. A modified Delphi approach was adopted.

Results: A total of 14 statements have been discussed. Consensus was reached on 11 *strong recommendations* and 2 *weak recommendations*. In one case, where consensus could not be agreed upon, no recommendation could be provided.

Conclusions: Management of SAH in a non-specialized setting and early transfer are difficult and may have a critical impact on outcome. Clinical advice, based on multidisciplinary consensus, might be helpful. Our recommendations cover most, but not all, topics of clinical relevance.

Keywords: Subarachnoid hemorrhage, Management, Transfer, Spoke center

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Background

Spontaneous aneurysmal subarachnoid hemorrhage (SAH), very often from the rupture of an intracranial aneurysm, is a neurological emergency associated with high morbidity and mortality worldwide [1–3]. The sudden intracranial bleeding causes a dramatic increase of intracranial pressure (ICP), a drop of cerebral perfusion pressure (CPP), and a cerebral blood flow (CBF) reduction. This transient global cerebral ischemia may have serious consequences [2–5]. After SAH, the main goal of neurocritical care is to prevent secondary brain injury [4, 6]. In particular, aneurysmal rebleeding, occurring more frequently within the first 24 h after SAH, increases the risk of mortality and poor clinical outcome [2, 3, 7, 8]. Rapid aneurysm securing by endovascular or neurosurgical treatment is therefore essential [9, 10]. Definitive aneurysm treatment and ventricular drain, which is often necessary, can only be performed in a specialized center. As a consequence, patients admitted to nonspecialized centers need to be transferred to a referral hospital as soon as possible [9, 10].

At present, only few aspects of SAH management are supported by high-quality studies, and most management principles are based on weak evidence [6, 9, 10]. This is especially true regarding the management of SAH patients in the hospital without neurosurgical/neurointerventional facilities and the transfer to referral hospitals. To address this issue, we created a consensus of experts endorsed by the Italian Society of Anesthesia and Intensive Care (SIAARTI). The specific aim of this consensus was to provide recommendations on the following:

- The early management of SAH patients admitted to the hospital without neurosurgical/neurointerventional facilities and
- The transfer to referral hospital for aneurysm's definitive treatment.

Methods

Panel selection and governance

The multidisciplinary consensus panel was composed of 16 voting physicians, a methodologist (CR) and two advisory board members (GC and NS) selected for their established clinical and scientific expertise in the management of SAH patients with different specializations: anesthesia/intensive care, neurosurgery, and interventional neuroradiology. The SIAARTI endorsed the project and supervised the methodology and structure of the consensus. The consensus was led by a steering committee (EP, FR and CR) who (a) conceived the project establishing the objectives, (b) organized and set the agenda for the voting of recommendations, (c) ensured

communications within the panel, and (d) drafted the report.

Delphi process

Following a non-systematic review of the literature, the steering committee identified the domains and generated a list of questions to be addressed by the panel. The initial list of statements was formulated and distributed to the panelists 1 week prior to every Delphi round in order to allow modifications or additional statements. The modified iterative Delphi process was conducted using online tools [11, 12]. In a preliminary step, questions were circulated. Based on the initial answers and on comments/suggestions by the voting members, ambiguities and inconsistencies in the questionnaire were identified and corrected, generating a refined question set for subsequent voting rounds. We used an iterative approach; members were informed of the degree of consensus reached on the initial question round and asked to reconsider agreement or disagreement. Then, based on the answers collected at the third stage, statements for practical advice were proposed. The objective was to reach consensus, not necessarily unanimity.

The analysis of voting results was performed by a non-voting experienced methodologist (CR). A decision rule was predefined to ascertain the degree of consensus required to provide a recommendation. Statements were classified as a *strong recommendation*, *weak recommendation*, and *no recommendation* when respectively > 85%, 75–85%, and <75% of votes were in favor.

Terminology

In the following statements, a center without appropriate resources for aneurysm treatment both in personnel (cerebrovascular neurosurgeons, endovascular neuroradiologists, and neurointensivists) and/or technological facilities for diagnosis and therapy is indicated as Spoke. A specialized, high-volume center with all necessary facilities and staff available 24 h/day is, on the contrary, considered as Hub.

These terms refer to a well-coordinated “Hub and Spoke” system, where communications and cooperation are optimal. Our recommendations, however, may apply also to different situations, where a system has not yet been implemented. In that case, Hub and Spoke are simply indicating hospitals with different equipment and staff.

Results

The consensus provided a total of 14 statements. Consensus was reached on 13 topics, leading to 13 corresponding recommendations (Table 1): 11 were *strong recommendations*, endorsed by more than 85% of participants, while 2 were *weak recommendations*, supported

Table 1 List of consensus recommendations

No.	Recommendation	Level
1	We recommend that all salvageable spontaneous SAH patients (i.e., patients who may recover, at least to some extent, with appropriate treatment) admitted in a Spoke center be rapidly transferred to a Hub center after hemodynamic and respiratory stabilization.	Strong recommendation
2	We recommend using a telemedicine service for image transfer from the Spoke to the Hub center.	Strong recommendation
3	We recommend that the transfer of SAH patients should be performed by a physician with: experience in advanced airway management and life support strategies and basic knowledge in neurocritical care (i.e., medical management of cerebral swelling, herniation).	Strong recommendation
4	We recommend sedation, intubation and mechanical ventilation for SAH patients in coma (Glasgow Coma Scale (GCS) score ≤ 8) and/or with inadequate airway protection or respiratory failure.	Strong recommendation
5	We recommend sedation, intubation, and mechanical ventilation also for SAH cases with severe agitation, if this persists despite mild sedation and pain control.	Weak recommendation
6	We recommend, in poor-grade SAH patients needing transfer to the Hub center, an invasive monitoring of arterial blood pressure (ABP) in addition to the standard cardiorespiratory monitoring (electrocardiogram (ECG), heart rate (HR), peripheral oxygen saturation (SpO_2) and end-tidal carbon dioxide ($ETCO_2$)).	Strong recommendation
7	We recommend, to avoid aneurysmal rebleeding and to ensure an adequate CPP, the maintenance of systolic arterial pressure (SAP) between 120 and 160 mmHg. It is also reasonable to individualize the target considering patient's clinical history (i.e., arterial hypertension) and/or radiological signs of intracranial hypertension.	Strong recommendation
8	We recommend the maintenance of SAP values close to the lower limit (120 mmHg) in SAH patients without a history of arterial hypertension and/or radiological signs of elevated ICP.	Strong recommendation
9	We recommend the maintenance of SAP values close to the upper limit (160 mmHg), avoiding fluctuations, in SAH patients with a history of arterial hypertension and/or radiological signs of elevated ICP.	Strong recommendation
10	We recommend the maintenance of a platelet (PLT) count $> 100,000/mm^3$ in all salvageable SAH patients, possibly candidates for neurosurgical intervention.	Strong recommendation
11	We recommend maintaining a prothrombin time (PT)/ activated partial thromboplastin time (aPTT) value < 1.5 the normal control in all salvageable SAH patients.	Strong recommendation
12	We recommend the early reversal of anticoagulants drugs in all salvageable SAH patients.	Strong recommendation
13	We recommend against the utilization of routine tranexamic acid for a short-term therapy before aneurysm treatment to prevent rebleeding of cerebral aneurysm/s.	Weak recommendation
14	We are unable to provide any recommendation regarding the use of routine seizure prophylaxis in all SAH patients.	No recommendation

Abbreviations: SAH subarachnoid hemorrhage, ICP intracranial pressure, GCS Glasgow Coma Scale, ABP arterial blood pressure, ECG electrocardiogram, HR heart rate, SpO_2 peripheral oxygen saturation, $ETCO_2$ end-tidal carbon dioxide, CPP cerebral perfusion pressure, SAP systolic arterial pressure, PLTs platelets, PT prothrombin time, aPTT activated partial thromboplastin time.

by 75–85%. The consensus flow chart was reported in Fig. 1. We were unable to reach consensus in one case. The consensus recommendations are listed below with the percentage of agreement.

Recommendation 1

We recommend that all salvageable spontaneous SAH patients (i.e., patients who may recover, at least to some extent, with appropriate treatment) admitted in a Spoke center be rapidly transferred to a Hub center after hemodynamic and respiratory stabilization (agreement: 87%, strong recommendation).

Recommendation 2

We recommend using a telemedicine service for image transfer from the Spoke to the Hub center (agreement: 100%, strong recommendation).

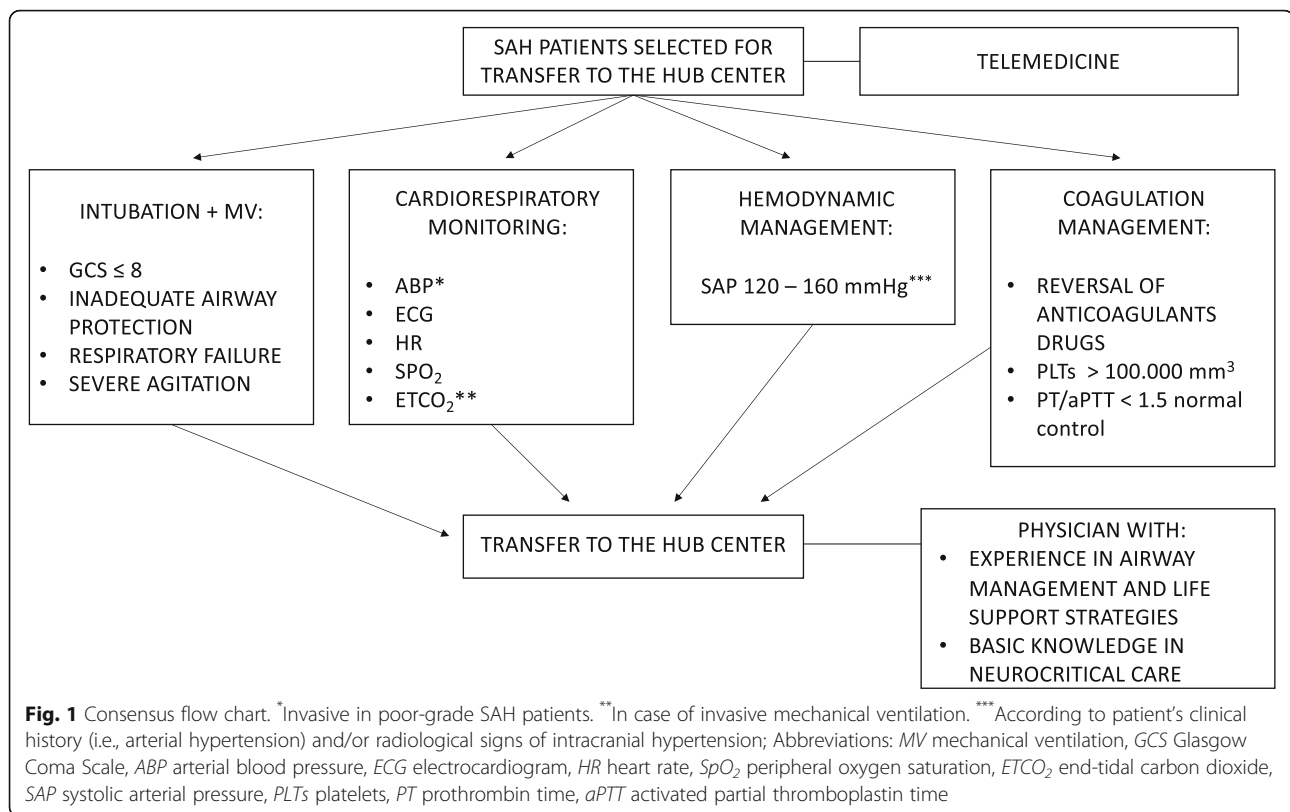
Recommendation 3

We recommend that the transfer of SAH patients should be performed by a physician with:

- Experience in advanced airway management and life support strategies and
- Basic knowledge in neurocritical care (i.e., medical management of cerebral swelling, herniation) (agreement: 93%, strong recommendation)

Recommendation 4

We recommend sedation, intubation, and mechanical ventilation for SAH patients in coma (Glasgow Coma Scale (GCS) score ≤ 8) and/or with inadequate airway protection or respiratory failure (agreement: 93%, strong recommendation)



Recommendations 5

We recommend sedation, intubation, and mechanical ventilation also for SAH cases with severe agitation, if this persists despite mild sedation and pain control (agreement: 81.5%, weak recommendation).

Recommendation 6

We recommend, in poor-grade SAH patients needing transfer to the Hub center, an invasive monitoring of arterial blood pressure (ABP) in addition to the standard cardiorespiratory monitoring (electrocardiogram (ECG), heart rate (HR), peripheral oxygen saturation (SpO₂), and end-tidal carbon dioxide (ETCO₂)) (agreement: 93%, strong recommendation).

Recommendation 7

We recommend, to avoid aneurysmal rebleeding and to ensure an adequate CPP, the maintenance of systolic arterial pressure (SAP) between 120 and 160 mmHg. It is also reasonable to individualize the target considering patient's clinical history (i.e., arterial hypertension) and/or radiological signs of intracranial hypertension (agreement: 93%, strong recommendation).

Recommendation 8

We recommend the maintenance of SAP values close to the lower limit (120 mmHg) in SAH patients without a

history of arterial hypertension and/or radiological signs of elevated ICP (agreement: 87%, strong recommendation).

Recommendation 9

We recommend the maintenance of SAP values close to the upper limit (160 mmHg), avoiding fluctuations, in SAH patients with a history of arterial hypertension and/or radiological signs of elevated ICP (agreement: 87%, strong recommendation).

Recommendation 10

We recommend the maintenance of a platelet (PLT) count > 100,000/mm³ in all salvageable SAH patients possibly candidates for neurosurgical intervention (agreement: 93%, strong recommendation).

Recommendation 11

We recommend maintaining a prothrombin time (PT)/activated partial thromboplastin time (aPTT) value < 1.5 the normal control in all salvageable SAH patients (agreement: 93%, strong recommendation).

Recommendation 12

We recommend the early reversal of anticoagulant drugs in all salvageable SAH patients (agreement: 93%, strong recommendation).

Recommendation 13

We recommend against the utilization of routine tranexamic acid for a short-term therapy before aneurysm treatment to prevent rebleeding of cerebral aneurysm/s (agreement: 81%, weak recommendation)

Recommendation 14

We are unable to provide any recommendation regarding the use of routine seizure prophylaxis in all SAH patients (agreement: 69%, no recommendation).

Discussion**Patient transfer to the Hub center**

Aneurysmal rebleeding is more frequently observed during the first 24 h after SAH and is associated with high mortality rates [2, 3, 7, 8]. Therefore, after SAH diagnosis, it is of paramount importance to prevent aneurysm rebleeding by transferring the patient to a specialized center to allow the rapid treatment of the aneurysm [9, 10]. The management of SAH patients in high-volume centers, with experienced staff (neurovascular surgeons, endovascular neuroradiologists and neurocritical care specialists), is associated with improved neurological outcomes [9, 10, 13, 14]. As recommended also by recent guidelines [15], the transfer should be performed after cardiorespiratory stabilization. Some panel members, during the consensus development, suggested that a quick, clear, and complete communication (regarding medical information, transport timing, etc.) between hospitals and within the Hub center (activation of neurosurgeons, neuroradiologists, and neurointensivists) is advisable in these cases. The availability of shared protocols could be helpful in this regard and should be encouraged.

The transfer of radiological images by a web-based software allows neurosurgical consultation between hospitals. This procedure, also preventing unnecessary transfers, is considered life and time-saving as well as cost-effective [16, 17]. All panel members agreed on this point. Therefore, telemedicine should be encouraged in this setting.

SAH patients can be admitted to the Spoke hospital with a range of neurological severity (from headache to coma) and with a number of extracranial problems (i.e., neurogenic pulmonary edema, Takotsubo cardiomyopathy) [2, 3, 6]. SAH patients can also deteriorate at any time during the transfer (rebleeding, seizures, etc.). Therefore, as suggested also by other guidelines [15], these patients should be accompanied during the transfer by a physician with expertise in airway management, life support strategies, and basic knowledge about neurocritical care. Considering the abovementioned points and also according to recent guidelines [15], an adequate cardiorespiratory monitoring seems to be fundamental

for the safety of the patients. In particular, invasive BP monitoring, allowing a precise and continuous BP estimation, is preferable, especially in unstable or poor-grade SAH. In addition, during the consensus rounds, some panelists suggested that a standard and basic cardiorespiratory monitoring (ECG, HR, SpO₂, and noninvasive BP (NIBP)) should be utilized during the transfer also in mild cases. However, the placement of an arterial line should not delay excessively patient's transfer, and NIBP can be considered a valid alternative in case of difficult arterial puncture.

Airway management

Comatose SAH patients (GCS \leq 8), unable to protect their airway and/or cardiorespiratory compromise, require tracheal intubation and mechanical ventilation [6, 16]. These maneuvers should also be reserved to patients who remain very agitated despite mild sedation and pain control [6, 16]. Tracheal intubation needs to be performed carefully, with adequate analgo-sedation, to avoid increase in ABP that can facilitate rebleeding or severe hypotension with possible cerebral hypoperfusion [16]. The panelists, in case of mild sedation and pain control, suggested the utilization of drugs with a short half-life and are easily titratable in order to allow a reliable neurological examination.

Hemodynamic and coagulation management for rebleeding prevention

Important ABP fluctuations can be dangerous after SAH. High values of ABP can increase the risk of rebleeding (by increasing transmural pressure), and low values can exacerbate secondary brain injury reducing CPP especially in case of intracranial hypertension [6, 18, 19]. Moreover, it is important to keep in mind that in case of chronic arterial hypertension, the cerebral autoregulation curve is shifted to the right [20], and these patients are more likely to experience cerebral hypoperfusion, especially in case of elevated ICP [10, 20]. While there are various indications with regard to maintaining an SAP < 160 mmHg, little is known about the minimum value of SAP to be tolerated [9]. The panel agreed, as a safe lower SAP, a value of 120 mmHg being the upper limit of normal SAP [20]. ABP values, before aneurysm treatment, should be also individualized considering patient's past medical history and the risk of intracranial hypertension.

Coagulopathy can promote rebleeding [21]. Moreover, some SAH patients may be in therapy with antithrombotic and anticoagulant drugs for preexisting pathologies [18, 21]. In this case, a PLT count greater than 100,000/mm³ (especially in patients needing neurosurgical intervention) as well as a PT/aPTT value < 1.5 the normal control seems to be reasonable to prevent complications.

These recommendations, in addition to the reversal of anticoagulant drugs, are in accordance with previous recommendations [21, 22]. In addition, any physician involved in the management of these patients should be aware of the strategies regarding the reversal of anticoagulation, also considering the increase in the utilization of novel oral anticoagulants (NOACs) [18, 21]. The utilization of point-of-care (POC) tests (i.e., thromboelastometry (TEG) and rotational thromboelastography (ROTEM)), although not easily available (especially in peripheral hospital), can be useful to guide the reversal of these drugs [23]. The most recent American Heart Association (AHA) guidelines for SAH management consider reasonable a short-term (< 72 h) therapy with tranexamic acid (1 g every 6 h) or aminocaproic acid to reduce the risk of early rebleeding especially in patients with an unavoidable delay in aneurysm obliteration and in the absence of medical contraindications considering the increased risk of thrombosis [9]. Recently, the data from the ultra-early tranexamic acid after subarachnoid hemorrhage (ULTRA) study (a multicenter randomized controlled trial) showed that an ultra-early (as soon as possible), short-term tranexamic acid treatment (1 g bolus followed by a continuous infusion of 1 g terminated immediately before aneurysm treatment, or 24 h after start of the medication) did not improve clinical outcome at 6 months [24]. In this study, the median time from computed tomography (CT) scan to the start of aneurysm treatment was 14 h. Our recommendation refers mainly to this study. However, some panel experts suggested that, unfortunately, in some centers, the aneurysm treatment cannot be performed within 24 h or as fast as in the ULTRA study.

Finally, we found no consensus on the prophylactic use of antiepileptic therapy in patients with SAH. While the most recent guidelines suggest to avoid the prophylactic administration of antiepileptic drugs in SAH patients [9], part of the consensus panel consider it as clinical practice, especially in poor-grade SAH and in case of clinical or radiological features which increase the risk of seizures (i.e., aneurysm's location, presence of hematoma).

Limitations

These recommendations are based on the clinical expertise and knowledge of the participants. We deliberately did not base our statements on systematic literature reviews because of the lack of evidence (previously underlined) and in favor of simple, basic topics that are rarely subject to investigation.

Important aspects of diagnosis and care are not covered: for the sake of simplicity, we did not address important topics as the neurologic examination, the diagnosis of SAH, diagnosis and treatment of pulmonary

and cardiac consequences of SAH, etc.. Accordingly, we did not explore the design of a well-organized Hub and Spoke system.

Conclusions

The aim of this consensus was to create recommendations to support clinician's decision-making in the management of SAH patients in Spoke hospitals. Due to insufficient evidence, our recommendations do not represent a mandatory standard of practice but are suggestions by clinicians to clinicians.

Abbreviations

SAH: Subarachnoid hemorrhage; SIAARTI: Italian Society of Anesthesia and Intensive Care; ICP: Intracranial pressure; CBF: Cerebral blood flow; DCI: Delayed cerebral ischemia; GCS: Glasgow Coma Scale; ABP: Arterial blood pressure; BP: Blood pressure; ECG: Electrocardiogram; HR: Heart rate; SpO₂: Peripheral oxygen saturation; ETCO₂: End-tidal carbon dioxide; CPP: Cerebral perfusion pressure; SAP: Systolic arterial pressure; PLTs: Platelets; PT: Prothrombin time; aPTT: Activated partial thromboplastin time; NIPB: Noninvasive ABP; POC: Point-of-care; TEG: Thromboelastometry; ROTEM: Rotational thromboelastography; AHA: American Heart Association; ULTRA: Ultra-early tranexamic acid after SAH; CT: Computed tomography

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Authors' contributions

See Methods section. The authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate

Not applicable.

Competing interests

The authors declare that they have no conflicts of interests.

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